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AdvaMed
Advanced Medical Technology Association

July 30, 2004

Division of Dockets Management (HFA–305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852.

Re: Docket: 2004N-0181 - Critical Path Initiative; Establishment of Docket

Dear Sir/Madam:

The Advanced Medical Technology Association (AdvaMed) is pleased to submit the attached comments on the subject docket. AdvaMed is the world's largest association representing manufacturers of medical devices, diagnostic products, and medical information systems. AdvaMed's more than 1,100 members and subsidiaries manufacture nearly 90 percent of the $75 billion of health care technology products purchased annually in the United States, and more than 50 percent of the $175 billion purchased annually around the world.

AdvaMed members range from the largest to the smallest medical technology innovators and companies. Nearly 70 percent of our members have fewer than $30 million in sales annually.

We expect this FDA effort will result in improved times to market for many products, and we are especially confident of the benefits that may accrue if the recommendations contained in our comments are implements.

We appreciate the opportunity to contribute to this effort. Please direct any questions or requests for additional information to Bernie Liebler (bliebler@advamed.org, 202.434.7230)

Sincerely

Bernie Liebler
Director
Technology and Regulatory Affairs

2004N-0181

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AdvaMed Comments on the FDA Critical Path Initiative

AdvaMed compliments FDA on this effort to develop an organized approach to identifying impediments to and improving the process by which we bring medical products to market.[1] We remark particularly on the recognition that there is more to speeding up the overall process of getting a product to market than simply revising the FDA review and approval processes.[2] We believe that this very important document opens doors to a number of activities that will benefit industry and FDA alike—and most importantly patients. In preparing these comments, we have had a number of informal discussions with FDA staff, and we believe that many of our recommendations should be easy to implement.

Our initial reaction upon reading the FDA report was to question the assertion that all approvals are declining. The report states in several places that its findings apply to drugs, biological products, and medical devices, but the assumption that there is stagnation across the healthcare products is based on metrics for drugs and biological products only, and the graph illustrates that there has been a steady 10-year decline in submissions for new drug and biological products. We reviewed the corresponding data for new medical device submissions (i.e., PMAs and IDEs as an indicator of future PMA submissions) and informed FDA that our review of the data shows that there has been a easily observable increase in both PMA and IDE submissions over the same 10-year period. The significance of this finding is that we believe the factors driving medical device innovation may differ considerably from those that produce new drugs and biological products. After we provided this information to FDA, FDA presentations reflected a more accurate picture of medical device innovation statistics.

Beyond the mere numbers of submissions and approvals, we were struck by the poor fit between the development model described in the report and the development model employed by the medical device industry. Figure 4, The Critical Path for Medical Product Development, has been the linchpin of most FDA presentations, and is central to the FDA report. The figure presumes the products across the agency follow a similar development track. While we recognize the need to focus this report across an extremely broad spectrum of products, we are concerned because the development model presented does not accurately represent the medical device and diagnostics industries.

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[2] While we understand that FDA "approves" only PMA devices and that other devices are "cleared," we use the term "approve" generically in this document.

FDA has a long-standing, well-defined *model* for drug approvals. Because this "drug model" has such a long history, the public, including legislators, is very familiar with it and tends to conclude that it applies to all FDA-regulated medical products. In fact, the paragraph following the figure states, "Medical device development is generally much more iterative, so that prototypes often build on existing technologies." While this comment is accurate, we believe it tells only part of the story.

Drugs are frequently "discovered." In other words, a substance that could have beneficial therapeutic effects is recognized. The development process and associated clinical trials then serve to demonstrate that the substance is truly beneficial and safe for use in humans and animals. Fundamental technologies and the medical devices that incorporate them are typically not "discovered"; they are designed. Moreover, utilizing a risk management process, manufacturers continue to modify the designs throughout the product life cycles.

Medical device developers can usually determine precisely what they expect a device to do, and they design the appropriate functionality into it. Clinical data collection and clinical trials then are intended to demonstrate that the designed device safely performs its intended use. During the various stages of device testing, the data collected on device performance are fed back to the designers to make any necessary or appropriate changes. Thus, the device evolves slowly throughout the development process. This process of continual improvement through feedback continues after the device is approved (cleared) and marketed, leading to future generations of the device.

In many cases, manufacturers of medical devices adapt well-developed technologies previously developed for non-medical purposes. The application of lasers in medical devices is a good example here. In these instances, the device development process can potentially be far less complex because much of the basic research on the technology has already been done.

Furthermore, many device applications are for improvements, modifications, or combinations of existing devices rather than for something that has never before existed. Frequently, such devices take a significant step forward in either treatment or diagnosis. For example, Automatic External Defibrillators (AED), an application of sophisticated electronics with built-in feedback loops to a well-known technology, represents an extraordinary step. Now, a completely untrained individual can apply this life-saving technology in places where it was never before available (e.g., airplanes, airports, offices). In his keynote address at a National Library of Medicine workshop in 2000, Robert W. Mann of the Massachusetts Institute of Technology (MIT), quoted Edward B. Roberts, of MIT's Sloan School, who described the process as follows; innovation in medical devices is usually based on engineering problem-solving by individuals or small firms, is often incremental rather than radical, seldom depends on the results of long-term research in the basic sciences, and generally does not reflect the recent generation of fundamental new knowledge.[3]

[3] "Innovation and Invention in Medical Devices," National Academy Press, 2001, Washington, D.C.

We do not intend to disparage the drug model. We want simply to emphasize that it does not fit devices very well. Thus, the discussion in the report must be somewhat tempered when applied to medical devices, and we need to focus beyond the science onto some of the procedural matters that FDA can easily address. The needs for translational research are not quite as apparent or pressing. We suggest that for medical devices there is a need for both translational research and for revision and bolstering of some of the regulatory tools that are already in place.

In the discussion below, we have not followed the format requested in the *Federal Register* Notice. We believe that strengthening and perfecting some of the regulatory tools already in place will be as important as translational research in moving medical devices through the system more quickly. Thus, we are recommending a number of efforts, some rather broad, some specific. Some will require several separate activities to fulfill the concept. While they are generally regulatory in nature, they also encompass some aspects that will require both scientific and analytical work. We believe, however, that each of these recommendations will, if carried to completion, lead to improved product development times.

Medical Devices Development and Approval Model

Medical Devices Model Development - Develop a formal model to describe the medical device process *

As we pointed out above, there is a well-defined drug model that drives many FDA activities and certainly drives a lot of the legislative perception of FDA activities. Because many people both in the FDA and in the Congress have some level of understanding of the drug model, they tend to attribute it to all of the FDA approvals processes. The result is one-dimensional discussions of multidimensional issues. We would like to encourage a joint effort among FDA, academia, NIH and the medical device industry to develop a formal "device model." Since there are many levels of devices in terms of both complexity and risk, we believe that the model will be complex (possibly a multiplicity of simple models addressing different types of devices with differing levels of risk and complexity). We also envision this model as describing the complete system, including research, development, regulatory requirements, and commercialization. For the model to be complete, it should also address payment issues, as many medical devices, particularly those used in hospitals, cannot be sold commercially until third party payers approve them for payment.

We view this as a relatively long-term effort that will require input from scientists, clinical experts, regulatory experts and payment experts. We also believe that the creation of such a formal model will facilitate many discussions between FDA and

* Note: * indicates a topic that may also be relevant to Secretary Thompson's Task Force on Medical Innovation Technology

industry and between industry and FDA and Capitol Hill. It should also ease the pathway for new products developed by companies new to medical devices.
Some of the issues that this model should cover are:

a. Research and development
b. Needs for clinical data/clinical studies
c. Approval/clearance process
d. Feedback loops including post market data collection
e. Device distinctions – Tool Devices, Therapeutic Devices, IVDs (special class of Tools). Tools are devices that perform particular, well-defined functions that are independent of any particular clinical outcomes, e.g., scalpels cut; they must be sterile and sharp. We discuss this idea further in Item 5, where we suggest that (IVDs) FDA could approve certain in vitro diagnostic devices without FDA's requiring demonstration of the medical applicability of the test.

Finally, given the explosion of technological advances and the proliferation of medical information that drives treatment decisions, this work needs to address whether the current regulatory models will be an effective tool to regulate these new technologies while allowing rapid patient access or whether they will act as barriers to such patient access

Feedback - Document the formal and informal feedback mechanisms critical to device development.

As we have discussed, the device development process is highly iterative. Another way to say the same thing is that the process relies heavily on feedback. The feedback includes both premarket information, e.g., data obtained from the manufacturing process, to postmarket information, such as adverse event reports. It is likely that the in-house "loops" are well developed. However, the external mechanisms are less well organized and generally less effective. In January 2004, JAMA published an article co-authored by Rosalie Bright of FDA that examined several methods of hospital surveillance of adverse events.[4] The report observed that the various surveillance methods examined yielded different and inconsistent results. It would be worthwhile to pursue a discussion of post market surveillance methods while addressing feedback loops, since manufacturers gain a great deal of useful information from post market sources, both formal and informal.
A project to define the feedback paths and iterations related to medical device development is likely to result in a better understanding of a key element of the development process. We believe that this could lead to post market reporting that would be less burdensome and more informative than the current systems.

We also believe that better understanding of the feedback mechanism could provide a means to create more effective post market studies that would benefit all parties. Current post market studies are frequently too extensive and expensive and do not recognize the changing use patterns that occur as the clinical community gains experience with a new

[4] Samore, Matthew H., et.al., "Surveillance of Medical Device–Related Hazards and Adverse Events in Hospitalized Patients," *JAMA*. 2004;291:325-334

device. They also fail to take into account the rapid changes in medical devices, whereby one generation of a product may replace the previous next generation in as little as twelve months. As a result, companies rarely complete the studies, and they rarely provide valuable information for either the company or the agency. A good post market study should be a source of useful information for the manufacturer to use in its required risk management system, which is intended to assist the manufacturer in assuring the safety of current devices and guiding the development of device enhancements. There is clear room for improvement in this area, and a clear understanding of how post market reporting can fit into the product development cycle in an organized way should help rectify this situation.

Guidance Development – Develop an improved system for creating new guidance documents, revising/updating existing guidance documents, and getting more industry input in the earliest stages of guidance development.

Guidance documents are of great value to both industry and FDA staff. When a good guidance document is in place, the industry understands what the agency expects to see in a submission. Similarly, the FDA reviewer can be comfortable that most incoming submissions will be close to the mark in terms of appropriate content, Historically, there has been a need for more guidance than FDA has staff time to produce. Thus, many existing documents have fallen out-of-date and thus present little value to either industry or FDA. In addition, many existing and emerging technology areas and devices suffer from a lack of written guidance. This lack of current guidance makes it much more difficult for companies to provide FDA with the data and information they expect in submissions. This slows the approval process and can act as a significant barrier to companies just entering a particular field.

Unfortunately, the promulgation of the agency's Good Guidance Practices, intended to bring greater transparency to the process, may have had the inadvertent effect of slowing the development process. In recent years, FDA staff has been much more cautious about working with industry on guidance, even at the drafting stage. We believe that we need to develop mechanisms to permit FDA and industry members to work together, either formally or informally, to develop first drafts of guidance documents. Developing the first draft is the major hurdle in developing either guidance or a standard. Once a draft that has at least a first level of agreement is completed and made available for public comment, the process can flow much more smoothly and rapidly. We believe any efforts to expedite both the development of new and the revision of existing guidance documents would have dramatic positive impact on the development and availability of significant new medical technologies.
(See next Item.)

Use of Recognized Standards – Develop data summary templates for recognized consensus standards.

CDRH accepts declarations from manufacturers stating that their device complies with a recognized consensus standard, or will comply with that standard before it is released for sale. Declarations of Conformity relieve the manufacturer of the burden of submitting detailed data to support the conformance to the standard. However, the manufacturer must submit a data summary in place of the complete detailed data set as part of the Declaration of Conformity. To date, the number of manufacturers filing Declarations of Conformity is less than expected. While the explanation for this lack of response is complex, a part of the explanation may be the lack of guidance regarding these data summaries. We recommend that CDRH prepare a data summary template for each standard that it recognizes and publish it along with the data sheet on the recognition of that standard. This would ensure that both manufacturers submitting a Declaration of Conformity and the reviewer receiving it would have a common understanding of what is required. We believe that this recommendation ties in closely with our Item 2, as the availability of adequate FDA guidance documents facilitates the effective use of standards.

IVD ISSUES

Approve Lab Tests Based on Characterization of Analytes – When clinical significance of analytes is accepted by the medical community, approve in vitro diagnostic devices (IVDs) based on their ability to detect/quantify an analyte.

In a report dated March 2001, Deutsche Banc Alex. Brown estimated that "home brews"[5] accounted for 30 percent of the nearly $5.0 billion market for "life science reagents."[6] Others have estimated that the market share for home brews may be even higher. Research conducted by the Task Force on Genetic Testing suggests that 55.3 percent of non-profit clinical laboratories offering genetic testing services used tests developed in-house, as did 47.8 percent of biotechnology companies providing such services.[7]

Most laboratories that perform genetic testing use their own tests, which are unregulated by FDA.[8] In fact, according to FDA, in 2000, at least 301 clinical or research genetic tests were offered in the U.S.,[9] and 158 laboratories offered clinical tests.[10] Yet at the time, FDA had approved only six specific gene tests.[11]

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5 Home brews are diagnostic assays or tests created by clinical laboratories for use by that laboratory.

6 *See* Deutsche Banc Alex. Brown, LIFE SCIENCE REAGENT COMPANIES: HELPING DECIPHER THE GENETIC CODE 9 (2001).

7 National Human Genome Research Institute, *Final Report of the Task Force on Genetic Testing, Appendix 3. State of the Art of Genetic Testing in the United States: Survey of Biotechnology Companies and Nonprofit Clinical Laboratories and Interviews of Selected Organizations* 14 (1997).

8 Cystic Fibrosis FAQ, Genetics & Public Policy Center, http://www.dnapolicy.org/cf/faq.jhtml, (last visited April 12, 2004).

9 David W. Feigal, Jr., Center for Devices and Radiological Health, "Future Trends" (July 18, 2000) (presented before the AdvaMed Submissions Workshop, Washington D.C.).

10 *Ibid.*

11 *Ibid.*

With up to 80 percent of all healthcare decisions relying on clinical laboratory tests,[12] and up to 10 billion lab tests performed in the U.S. each year,[13] the risks posed by lab-made tests that lack FDA oversight cannot be overestimated.

Given the potential risks associated with the use of home brew tests, how does one account for their proliferation? Quite simply, tests developed and performed in labs do not require prior review by FDA, while tests developed by manufacturers and sold to labs do. Clearly, laboratorians believe that it is necessary to provide testing services for newly recognized analytes and for analytes that represent niche markets, and both laboratorians and the physicians who order tests are unwilling to wait for tests to go through the FDA review process. This suggests that FDA needs a much speedier process than is currently available for enabling tests that identify new analytes to get to market.

In many cases, particularly when home-brew tests have proliferated, there is ample evidence of the clinical significance of the analyte. When such evidence exists, FDA could grant marketing permission for new diagnostics based on characterization of analytes rather than on full clinical testing. The requirement for FDA approval would apply to both manufacturer- and lab-developed tests. This would provide a greater degree of FDA oversight than at present and could assure that tests, wherever developed, comply with FDA requirements for registration and listing, labeling and instructions for use, adverse event reporting, and good manufacturing practices. Previously, when confronting this challenge, FDA took the position that it lacked the resources to deal with the influx of applications that would result. Currently, however, FDA has the ability to collect user fees for diagnostic reviews, which could provide the needed additional resources.

Alternatively, should FDA adhere to its current position that it will not regulate tests developed and performed by clinical laboratories, easing of submission requirements would enable manufacturers to obtain marketing clearance with the same type and quantity of data that laboratories currently collect prior to offering a new testing service. In this way, FDA would assure a level playing field and would enable manufacturers, for who the FDA approval process provides the added assurance of safety and effectiveness, an incentive to develop new tests rapidly.

Informed Consent and the Use of Leftover or Banked Samples – Develop guidelines for waiving informed consent and IRB review for studies using leftover or banked samples that are unlinked or unidentified.

Historically, IVD companies have utilized leftover or banked samples to characterize the performance of their products and to control manufacturing processes. These samples have been collected by laboratories when patients were referred for specific testing and

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12 *See* Nancy Williams, *How Reliable is Laboratory Testing?*, www.labtestsonline.org/understanding/features/reliability.html (last modified May 19, 2003).

13 *Ibid.*

have typically been characterized by a medically accepted test or method. There are many advantages to using these samples, particularly for those diseases or conditions where positive samples appear infrequently, e.g., atypical pneumonia caused by M. pneumoniae. By using banked samples, a company may be able quickly to demonstrate a test's sensitivity and specificity, rather than waiting several years to enroll a large enough number of test sites to find positive patients.

Generally, studies that utilize leftover or banked samples require little if any personal health information to be transferred with the sample or the test result. These studies can typically be performed on unidentified, unlinked, limited data, or coded samples.[14] In its report issued in August 1999, the National Bioethics Advisory Commission (NBAC) determined that:

- "Research conducted with unidentified samples is not human subjects research and is not regulated by the Common Rule" (no IRB or informed consent necessary).
- "Research conducted with unlinked samples is research on human subjects and is ... eligible for exemption from IRB review" (IRB exempts study from review, no informed consent necessary).
- "When a study is of minimal risk, informed consent is no longer needed.... IRBs should operate on the presumption that research on coded samples is of minimal risk to the human subject if a) the study adequately protects the confidentiality of personally identifiable information obtain in the course of research, b) the study does not involve the inappropriate release of information to third parties, and c) the study design incorporates an appropriate plan for whether and how to reveal findings to the sources or their physicians should the findings merit such disclosure."

Although the NBAC report was referring to the Common Rule (45 CFR 46), and not to FDA's IRB and Informed Consent rules (21 CFR 50 and 21 CFR 56), the same principles should apply. The two rules should be consistent.

Based on this information, we recommend that FDA set guidelines for waiving IRB review and informed consent requirements for IVD studies that utilize leftover or banked samples that are either unidentified or unlinked. AdvaMed further suggests that FDA waive the informed consent requirements (but not the IRB review) for limited data or coded samples.

IVD Clinical Validation – Identify new approaches to clinical validation of molecular diagnostic devices.

[14] Limited data samples are those that include certain demographic information, as defined by HIPAA, but cannot reasonably be identified from that information. An unidentified sample is one that has no accompanying demographic information or identifying information or an individual sample that has been pooled with other samples so that it is no longer individually distinguishable.

Notwithstanding our comments regarding the speed to market of new IVD tests, including genetic tests, there may be situations in which clinical validation of a molecular test is necessary or desirable to support a product claim. Here, it would be beneficial to identify new approaches to clinical validation of molecular diagnostics. Such approaches could include:

a) The use of literature to establish or bridge clinical validity when supported by analytical claims,

b) Obtaining a statistically adequate number of specimens by phenotype, rather than genotype,

c) Statistical methodologies applied to existing literature, or

d) The use of DNA specimens collected from previously completed clinical trials for prospective clinical validation by blinding those genotyping the specimens from the clinical data under a pre-specified analysis plan.

IVD Reagent Accelerated Stability Model – Develop an accelerated IVD reagent stability model.

Develop an accelerated reagent stability model for establishing IVD reagent expiration dating. The current approach is based on real time data developed over an extended period (e.g., 2 years). For those products for which it is appropriate, an accelerated model based on real time data that are extrapolated to obtain reagent stability would expedite products to market.

IVD Risk-based Approaches to Process Validation – Develop risk-based approaches to process validation to expedite the availability of IVDs to address emergent diseases.

Risk-based approaches applied to areas of the IVD product development cycle, such as process validation, can expedite the availability of IVDs to address emergent diseases. Develop risk-based models for IVD process validation based on concepts, such as: (1) the use of components from other validated assays, (2) process point inspection (i.e., process points that through FMEA are traceable to critical product quality attributes) and test verification, in lieu of validation, or (3) validation plans designed for post-approval validation.

IVD Photostability Model – Develop a photostability model for IVD reagents.

Currently, FDA assesses IVD reagent photostability using the pharmaceutical model, resulting in data that are often difficult to interpret and apply. An IVD reagent photostability model, developed with input from appropriate stakeholders, would result in studies yielding more meaningful data and aid more rapid product development.

Test Development by CDC – Require CDC to follow the same process required of manufacturers for development of new tests for emerging pathogens.*

In several recent instances, most notably during the anthrax scare, the Centers for Disease Control and Prevention (CDC) have developed "home brew" diagnostic tests, distributed them to public health laboratories, and required the laboratories to use only those tests. CDC did not distribute these tests to privately owned laboratories, nor did they ask for or receive FDA clearance for these new diagnostic tests. In all cases, there were members of the IVD industry willing to and interested in developing similar tests. However, the CDC actions rendered it infeasible for them to do so.

While we respect the need to move quickly in times of public health emergencies, we find it unseemly for a federal agency to place itself in effective competition with private industry while circumventing the controls that would have affected similar products that industry developed. We recommend that HHS develop some internal interagency policies that would either require CDC to satisfy the same requirements that apply to industry for the same activities or take CDC out of the business of test development, except in those circumstances where industry does not or cannot develop the needed tests.

Education and Training

Develop standing mechanisms for educating reviewers on new procedures and new technologies. *

Technology is changing extremely rapidly, and it is difficult for FDA reviewers to remain current, not only with the technology itself, but also with the medical procedures for which the technology is employed. There needs to be a well understood, carefully designed system for providing the needed educational opportunities to the CDRH reviewers. This seems to be an ideal vehicle for collaboration among FDA, industry, and academia.

As part of the overall education/training effort, it would be worthwhile to investigate the possibility of setting up more forums like the National Cancer Institute's (NCI) National Forum on Biomedical Imaging in Oncology, which NCI, FDA, and NEMA sponsor jointly. According to the NCI website, "The National Cancer Institute (NCI) is committed to facilitating the translation of promising new discoveries into the clinic."[15] The site also explains that "The National Forum on Biomedical Imaging in Oncology (NFBIO) was created in 1999 to facilitate partnerships with the imaging industry and government agencies to address new biomedical opportunities and challenges in oncology, and to focus on the regulatory, coverage, and reimbursement issues for more developed and established technologies."[16] We believe that it would be fruitful to examine the possibilities of establishing similar entities in additional specialty areas.

Note: * indicates a topic that will also be relevant to Secretary Thompson's Innovation Initiative.

[15] National Cancer Institute Web site: http://otir.nci.nih.gov/ir/forum.html

[16] *Ibid.*

Clinical Trials and Data Collection

Off-Label Use – Develop guidelines permitting companies to utilize data collected in formal studies of off-label device use to obtain approval for the appropriate indications and uses.

FDA does not regulate the practice of medicine. This is a long-standing principle that the FDA, the medical device industry, and the medical profession would like to maintain. Because of this fundamental principle, clinicians are free to apply medical products (drugs, biologics and devices) in ways and for purposes that neither the manufacturer nor the FDA considered during the application and approval process (provided the physician has determined the therapy to appropriate and necessary). In effect, this "off-label" use of medical products often serves as a proving ground for novel device applications (i.e., unfunded research and development).

In the spirit of the "least burdensome" principle, we recommend FDA be open to the use of data collected from independent, formal clinical trials to facilitate approval of new uses of existing medical devices. This becomes particularly important when an 'off-label' use has become so commonplace within the medical community that it has become the standard of care—thus making it impossible to enroll patients in a randomized clinical study that seeks to enroll one-half of the patients into a control group using an approved (yet obsolete) therapy or device.

There are circumstances in which it would be appropriate for FDA to accept data from an independent, formal clinical trial (or multiple such trials) to validate an off-label use, and there are circumstances where this would not be so. We believe that FDA could improve the flow of approvals for additional indications for already approved devices by defining reasonable guidelines for the use of independent rather than company-sponsored clinical trials.

Modeling – Identify areas where modeling is an appropriate substitute for data collection. *

As the power of computers has grown, it has driven the complexity and sophistication of computer modeling has increased substantially. In the appropriate circumstances, computer models could replace clinical data collection. The challenge here is to define those circumstances and to determine whether the cost of and the time required for model development make it worthwhile. In some instances, a good model could reduce both the cost of and time for an FDA approval. In other cases, the cost of the model itself could outstrip the savings, or, when technology is moving very rapidly, the time to develop the model could exceed the market life of the products.

We propose an effort to develop criteria to determine when models are appropriate. We believe that several areas have high potential and should be the first addressed: software, materials, toxicology, sterilization, and statistics.

Electronic Submissions – Develop a system for accepting electronic submissions in CDRH.

To our knowledge, CDRH currently scans paper submissions and circulates them internally in pdf format. It could save both companies and the agency time and resources, if there were a simple, straightforward way for companies to do (provide?) their submissions electronically. We recommend that CDRH collaborate with industry to develop an appropriate model for electronic submissions to CDRH, while ensuring that device manufacturers who submit to both CDRH and CBER do not need to maintain two separate systems.

Compare Science Requirements for Device Approvals – Compare the level of premarket scientific study required for device approval in the US and in other major regions with the postmarket success of the device to determine if there is a justification for any additional data required by FDA in the US. *

Many companies believe that FDA requires more studies (e.g., clinical trials, laboratory studies, animal studies) than other regions before approving or clearing a medical device. It would be valuable to perform a comparative study of the premarket science requirements and postmarket outcomes for PMA and 510(k) devices in the US and the EU. We suggest limiting this study to Europe for several reasons:

a. The EU is probably the region most comparable to the US in terms of culture, population, and medical care.

b. This may be a difficult study to complete, and it would be most sensible to limit the scope, at least at the beginning.

c. It is likely to be easier to collect the necessary data for Europe than for other regions.

The idea that FDA should use the "least burdensome" means to evaluate medical devices was included in the Food and Drug Administration Modernization Act of 1997. A comprehensive comparison study would look at both the quantity of data required for approval and the success of the device (e.g., use data, adverse events numbers and rates) to enable drawing a conclusion about whether the additional data translates to added patient safety or effectiveness. If the study can develop a meaningful, normalized comparison, and if it demonstrates a higher burden on US industry to produce clinical data, FDA would be bound by the "least burdensome" principle to open a discussion with industry on reducing that burden.

Applied Research at NIH

NIH should review and, if necessary, modify its grants review process to ensure that it addresses the device industry's applied research needs.

Historically, NIH has engaged primarily in basic research with an occasional foray into applied work. Recently, Congress established the National Institute for Biomedical Imaging and Bioengineering (NIBIB), which is the only NIH institute whose mission includes basic research, applied research, and translational research. The NIBIB Mission includes "promoting fundamental discoveries, design and development, and translation and assessment of technological capabilities in biomedical imaging and bioengineering, enabled by relevant areas of information science, physics, chemistry, mathematics, materials science, and computer sciences."[17] The NIBIB Mission also states that, "The Institute coordinates with the biomedical imaging and bioengineering programs of other agencies and NIH Institutes to support imaging and engineering research with potential medical applications and facilitates the transfer of such technologies to medical applications."[18]

We believe that NIBIB can play a key role in the success of the FDA Critical Path Initiative. In the medical devices area, much of the potential research resides in general areas of applied research that appear to fall within the NIBIB mission. For example, as software control becomes close to ubiquitous in electronic devices, an effective, efficient user interface becomes vital. Devices use fewer keys and buttons to control more functions. There is a need for more advanced human factors research to examine these newer, miniaturized interfaces, and we believe that NIBIB would be a natural home for this work.

We also believe that with the formation of NIBIB, the medical devices industry has a rare opportunity to develop a research agenda within NIH that can address some of the applied research that the industry would like to see. However, we do offer one caveat here. NIH has a long, distinguished history of performing basic health care research. Its grant approval process was set up to evaluate basic clinical research proposals, and the people who participate in it are used to that paradigm. To evaluate applied research proposals properly, they will need to approach them differently. Proposals for applied work deserving of funding would likely be scored low if one were to rate them using the same values one would use to rate a basic research proposal. The approval process will need to be significantly revised to refocus on proposals for applied work.

[17] NIBIB Mission statement
[18] Ibid.